

Claims:

1. A process for preparing (2S,3S,4R,5R)-2-(5-tert-butyl-[1,3,4]-oxadiazol-2-yl)-5-[6-(4-chloro-2-fluorophenylamino)-9H-purin-9-yl]-tetrahydrofuran-3,4-diol
5 (Compound A) as Polymorph I comprising:
- a) reacting 9-((3aR,4R,6S,6aR)-6-[5-tert-butyl-1,3,4-oxadiazol-2-yl]-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)-N-(4-chloro-2-fluorophenyl)-9H-purin-6-amine with trifluoroacetic acid/water; and
 - 10 b) neutralisation with aqueous methanolic ammonia solution at 25-50 °C over at least one hour; and
 - c) cooling to 0-5 °C, and optionally adding toluene.
2. A process for preparing (2S,3S,4R,5R)-2-(5-tert-butyl-[1,3,4]-oxadiazol-2-yl)-5-[6-(4-chloro-2-fluorophenylamino)-9H-purin-9-yl]-tetrahydrofuran-3,4-diol
15 (Compound A) as Polymorph I comprising:
- a) dissolving Compound A in N,N-dimethylformamide and water wherein the N,N-dimethylformamide:water ratio is in the range 2.5:1 to 1.5:1 and the dilution is at least 15 volumes; and
 - 20 b) initiating crystallisation by either:
adjusting the temperature to less than 25°C; or
adjusting the temperature to less than 30°C, and seeding with Polymorph I; and
 - 25 c) optionally, adding toluene.
3. A process for preparing (2S,3S,4R,5R)-2-(5-tert-butyl-[1,3,4]-oxadiazol-2-yl)-5-[6-(4-chloro-2-fluorophenylamino)-9H-purin-9-yl]-tetrahydrofuran-3,4-diol
30 (Compound A) as Polymorph II comprising:
- a) dissolving Compound A in N,N-dimethylformamide and water wherein the N,N-dimethylformamide:water ratio is in the range 2:1 to 1:2 and the dilution is at least 15 volumes; and
 - b) initiating crystallisation by either:
35 adjusting the temperature to greater than 35°C; and optionally seeding with polymorph II; and
 - c) optionally, adding toluene.
4. (2S,3S,4R,5R)-2-(5-tert-Butyl-[1,3,4]-oxadiazol-2-yl)-5-[6-(4-chloro-2-fluorophenylamino)-9H-purin-9-yl]-tetrahydrofuran-3,4-diol as Polymorph I in
40 spheronised habit.

5. (2S,3S,4R,5R)-2-(5-tert-Butyl-[1,3,4]-oxadiazol-2-yl)-5-[6-(4-chloro-2-fluorophenylamino)-9H-purin-9-yl]-tetrahydrofuran-3,4-diol as Polymorph I in a habit obtainable by a process of claim 1 or claim 2.
- 5 6. (2S,3S,4R,5R)-2-(5-tert-Butyl-[1,3,4]-oxadiazol-2-yl)-5-[6-(4-chloro-2-fluorophenylamino)-9H-purin-9-yl]-tetrahydrofuran-3,4-diol as Polymorph II in spheronised habit.
- 10 7. (2S,3S,4R,5R)-2-(5-tert-Butyl-[1,3,4]-oxadiazol-2-yl)-5-[6-(4-chloro-2-fluorophenylamino)-9H-purin-9-yl]-tetrahydrofuran-3,4-diol as Polymorph II in a habit obtainable by a process of claim 3.
- 15 8. A pharmaceutical composition comprising Polymorph I in a habit according to claim 4 or claim 5, and a pharmaceutically acceptable carrier and/or excipient.
9. A pharmaceutical composition comprising Polymorph II in a habit according to claim 6 or claim 7, and a pharmaceutically acceptable carrier and/or excipient.
- 20 10. Polymorph I in a habit according to claim 4 or claim 5 for use in decreasing plasma free fatty acid concentration; reducing heart rate; or treating ischemic heart disease, peripheral vascular disease, stroke, pain, CNS disorder, or sleep apnoea.
- 25 11. Polymorph II in a habit according to claim 6 or claim 7 for use in decreasing plasma free fatty acid concentration; reducing heart rate; or treating ischemic heart disease, peripheral vascular disease, stroke, pain, CNS disorder, or sleep apnoea.
- 30 12. A method of treating a patient suffering from a condition where there is an advantage in decreasing plasma free fatty acid concentration, or reducing heart rate, or treating a patient suffering from ischemic heart disease, peripheral vascular disease, stroke, pain, CNS disorder, or sleep apnoea comprising administering a therapeutically effective amount of Polymorph I of (2S,3S,4R,5R)-2-(5-tert-butyl-[1,3,4]-oxadiazol-2-yl)-5-[6-(4-chloro-2-fluorophenylamino)-9H-purin-9-yl]-tetrahydrofuran-3,4-diol in a habit according to claim 4 or claim 5.
- 35 13. A method of treating a patient suffering from a condition where there is an advantage in decreasing plasma free fatty acid concentration, or reducing heart rate, or treating a patient suffering from ischemic heart disease, peripheral vascular disease, stroke, pain, CNS disorder, or sleep apnoea comprising administering a therapeutically effective amount of Polymorph II of (2S,3S,4R,5R)-2-(5-tert-butyl-[1,3,4]-oxadiazol-2-yl)-5-[6-(4-chloro-2-fluorophenylamino)-9H-purin-9-yl]-tetrahydrofuran-3,4-diol in a habit according to claim 6 or claim 7.
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14. Use of Polymorph I in a habit according to claim 4 or claim 5 in the manufacture of a medicament for use in decreasing plasma free fatty acid concentration; reducing heart rate; or treating ischemic heart disease, peripheral vascular disease, stroke, pain, CNS disorder, or sleep apnoea.

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15. Use of Polymorph II in a habit according to claim 6 or claim 7 in the manufacture of a medicament for use in decreasing plasma free fatty acid concentration; reducing heart rate; or treating ischemic heart disease, peripheral vascular disease, stroke, pain, CNS disorder, or sleep apnoea.